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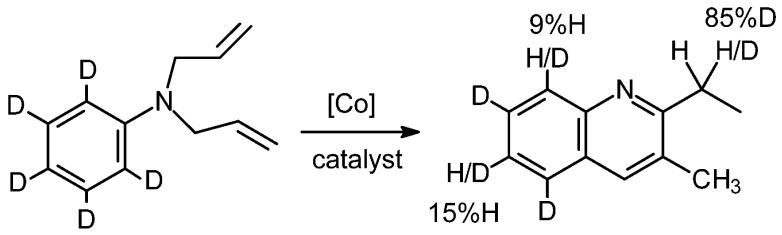

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Mechanistic Investigation of the Cobalt-Catalyzed Selective Conversion of Diallylanilines to Quinolines Involving C−N and C−H Activations

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Abstract: 2,3-Substituted quinolines were readily prepared from diallylanilines in good yields under mild conditions by using $Co_2(CO)_8$ as catalyst.[1,2] Regioselectivity has been explored by examining a series of electron-donating and electron-withdrawing functional groups at ortho, meta, and para positions of the diallylanilines. The results show that both steric and electronic effects influence the isolated yields. Electron-withdrawing groups inhibit the reaction. Solvent effects, temperature effects, and catalyst loadings have also been investigated. Isotopic labeling experiments were devised to permit delineation of the mechanism of reaction.

Introduction

The synthesis of nitrogen heterocycles, such as lactam,[3,4] pyrrole,[5,6] indole,[7,8] and quinoline derivatives, has been extensively developed for more than 100 years, because of the broad biological activities and pharmaceutical applications of these compounds. In particular, quinoline derivatives have been found to act as antimalarial,[9,10] antibacterial,[11] antiasthmatic, antihypertensive, and antiinflammatory[12] drugs. Quinolines are also important components in industrial antioxidants and dyes. In additional to medicinal and industrial applications, polyquinolines are found to undergo hierarchical self-assembly into nanostructures and mesostrutures with enhanced electronic and photonic properties.[13,14] New synthetic routes to quinolines would therefore have major impacts in the availability of these useful compounds.

There are five common methods used to prepare substituted quinolines: the Skraup reaction,[15] the Doebner−Von Miller reaction,[16] the Conrad−Limpach reaction,[17] the Friedlaender reaction,[18,21] and the Pfitzinger reaction.[22,23] All five reactions require environmentally unfriendly strong acids or bases, high temperatures, and harsh conditions, and quinoline yields are oftentimes low because of numerous side reactions. Several nonacidic transition metal-catalyzed processes were reported in the 1960s,[24] including rhodium,[25] ruthenium,[26−28] and biocatalyst systems.[29−33] Other interesting routes to quinolines have recently been reported.[34−36] For example, Katritzky has used a benzotriazole iminium salt to serve as a source of 'CH', which when reacted with *N*-arylimines completes the formation of the six-membered heterocycle ring.[35] Despite these advances, however, the development of new catalytic routes toward quinoline synthesis remains an active area of research. A novel cobalt-catalyzed selective conversion of diallylanilines to quinolines

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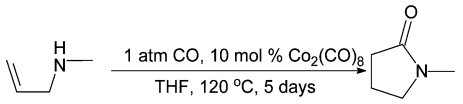
and the cross-coupling of arylimines with diallylanilines have been reported by our lab.[1,2] In this paper, we investigate the scope of the reaction with respect to allylanilines for quinoline synthesis, and the tolerance of different functional groups on the phenyl rings. The mechanism is also fully delineated based on isotopic labeling studies.

Results and Discussion

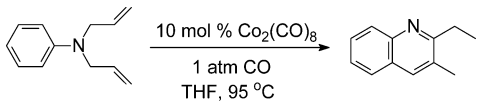
Reaction Scope. The current research stemmed from studies of metal carbonyls with aromatic compounds 'disposed' to make interesting heterocycles. Dicobalt octacarbonyl was discovered to be an effective catalyst to bring about carbonylative cyclizations to form lactams with simple allylamines. For example, when *N*-allylmethylamine was reacted with CO in the presence of $Co_2(CO)_8$, the lactam was formed in 95% yield as shown in eq 1.



(1)

Allylaniline was also found to react in the presence of $Co_2(CO)_8$ and 1 atm CO. Surprisingly, the reaction showed that CO was *not* incorporated into the products. NMR and GCMS examination of the reaction showed that only two products were formed, aniline and 2-ethyl-3-methylquinoline. Apparently, the C−N bond of allylaniline was cleaved by $Co_2(CO)_8$ and the three-carbon allyl group was incorporated into allylaniline to form the final quinoline product. The yield of quinoline was low because half of the allylaniline acted as an allyl source to complete the cyclization. Also, propane, propene, and H_2 were observed as byproducts.

Diallylaniline was immediately investigated as a substrate, and a clean reaction occurred in the presence of $Co_2(CO)_8$ and 1 atm CO. (An atmosphere of CO must be maintained to stabilize the catalytic cobalt species, without which a cobalt mirror is seen on the wall of the reaction ampule.) ^{1}H NMR spectroscopy showed that a 4:1 ratio of quinoline: aniline was formed (eq 2).

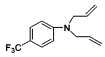
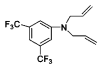


(2)

A range of diallylanilines were obtained by refluxing overnight commercially available anilines with 2.3 equiv of allyl bromide in 4:1 ethanol:water solution in the presence of sodium carbonate. A slight excess of allyl bromide was used because of the low boiling point of allyl bromide. A series of diallylanilines with electron-donating and electron-withdrawing groups in various positions were synthesized and were converted to quinolines using reaction conditions similar to those indicated in eq 1. The results are summarized in Table 1. Pure quinoline products were separated by column chromatography using 5−35% ethyl acetate/hexane as the eluent.

Electronic and Steric Effects. A series of 2-ethyl-3-methylquinolines were readily obtained, and substitutions were easily introduced at the 5-, 6-, 7-, and 8 positions. Entries 1, 4, 5, and 12 were compared under the same reaction conditions and after the same time. After 6 h, there was about 40% conversion of the starting material for entry 4, 60% conversion for entry 5, and no conversion for entry 12. It was also observed that even upon increasing the reaction temperature to 120 °C for 8 days, there was still more than 60% starting material present for entry 12. It is quite evident that introduction of an electron-donating group seems to favor the reaction, whereas an electron-withdrawing group severely inhibits the reaction. A similar trend was observed in that entry 2 reacted faster than entry 3 under the same reaction conditions, which can be attributed to the electron-donating group at the para position for entry 2. By comparing entries 1, 6, and 7, introduction of a methyl group at the ortho position can be seen to inhibit the reaction, and longer reaction time was required. These observations can be explained in that the methyl groups at ortho positions may both block ring closure to form the quinoline skeletons and disfavor the reaction. It was also observed that entry 4 was complete within 8 h as well as the highest isolated yield. The electron-donating methyl groups in meta positions favor the reaction and do not interfere sterically with ring closure. It seems that electronic effects predominate over steric effects. Entries 13 and 14 did not lead to the desired quinolines. This is possibly because of chelation with the reactive cobalt species, forming stable complexes that were unreactive.[37,38] One

Table 1. Yields for the Conversion of Diallylanilines to Quinoline Derivatives[a]

entry	substrate	product	T (°C)	% yield[b]
1			105	85(65)
2			105	73(32)
3			105	66(28)
4			105	87(67)
5			105	72(49)
6			105	40(17)
7			120	58(35)
8			120	48(29)
9			105	31(20)
10			120	50(26)
11			120	20(10)
12		--	120	--
13		--	120	--
14		--	120	--

[a] Yields at 100% conversion of the diallylaniline, using 10 mol % $Co_2(CO)_8$ in THF solvent under 1 atm CO in a closed ampule. Reaction time is 36−48 h. [b] NMR yield(isolated). The major byproduct is the corresponding aniline.

Table 2. Yields for the Conversion of Diallylaniline to 2-Ethyl-3-methylquinoline with Different Catalyst Loadings and Solvents (T = 105 °C, 1 atm CO, [diallylaniline] = 0.2 M)

entry	$Co_2(CO)_8$, %	solvent	% yield[a]	reaction time (h)
1	10	THF	85 (65)	~24
2	20	THF	92 (67)	8−24
3	50	THF	87 (63)	<2
4	10	toluene	79 (53)	~38
5	10	benzene	82 (58)	~21
6	10	hexane	60 (35)	>55

[a] NMR yield (isolated).

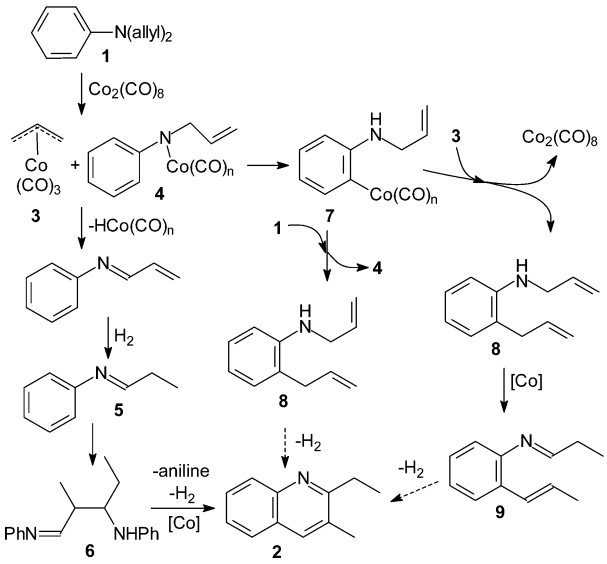
possible explanation for the increased efficiency with electron-donating groups is that these groups weaken the C−N bonds of the starting materials when placed on the aromatic rings, making the reactions faster. For entry 5, the second C−N might be cleaved, which would contribute to more aniline byproduct and lower isolated yield than for entry 4.

Reaction Condition Considerations. Different reaction conditions have been investigated in order to maximize the isolated yields of quinolines and to determine which conditions affect the reaction. Table 2 shows how the different catalyst loadings affect the reaction time. It was found that a negligible change in yield was observed as more catalyst was used, although the reaction was significantly faster. These observations are promising in that a small catalyst loading can catalyze the reaction despite long reaction times. Different solvents were also chosen to investigate solvent effects on the reaction, also summarized in Table 2. The reaction in hexane is much slower than reactions in other solvents, and the yield is also lower because of the poor solubility of the catalyst in hexane (some undissolved solid was observed at the beginning of the reaction). In the nonpolar solvent benzene, the reaction was as fast as in THF and the isolated yield was comparable to that obtained in THF.

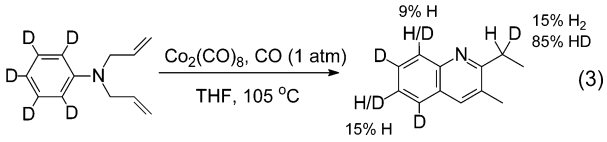
Mechanism Considerations. Both C−H activation and C−N activation are involved in this reaction in order to complete the ring closure. The reaction is complicated, with one C−N and five C−H bonds being broken, and two C−C, three C−H, and one H−H bond being formed, yet only one intermediate cobalt complex is observed. Monitoring the reactions by NMR spectroscopy did not produce significant information. The only two intermediates observed during the reaction were monoallylaniline and allylcobalttricarbonyl, which do not provide sufficient information to elucidate details of the catalytic process. A speculative reaction scheme was postulated in our earlier report[1] as shown in Scheme 1, but as outlined below, most of these pathways are inconsistent with mechanistic studies.

Mechanism of Quinoline Synthesis: Ortho C−H Activation. Apparently, one of the ortho protons of diallylanilines is cleaved from the arene ring by the cobalt catalyst in order to form a cyclized species. In order to investigate where these ortho protons on the phenyl group appear in the products, partially deuterated diallylaniline-d_5 was prepared by refluxing deuteroaniline with allyl bromide in 4:1/C_2H_5OD:D_2O solution. The reaction of diallylaniline-d_5 was examined by ^{1}H NMR spectroscopy and GCMS under similar reaction conditions to those

Scheme 1. Possible Pathways for the Catalytic Formation of Quinoline



used earlier. The reaction is much slower, and after 16 h there was little reaction, while the nondeuterated counterpart was converted completely into quinoline within this time. However, after 55 h, the reaction was essentially complete producing the results shown in eq 3. The presence of such a large isotope effect indicates that the aryl C−H/C−D cleavage must be one of the first steps in the reaction sequence. Notably, this implies that allyl C−N cleavage does not occur prior to C−H cleavage.



(3)

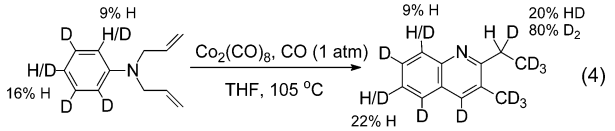
The distributions of deuterium were confirmed by ^{1}H NMR, ^{2}H NMR, ^{13}C NMR, HSQC, 2D COSY, and HMBC spectroscopy (Supporting Information). One of the ortho C−D bonds was activated, and the deuterium was selectively transferred to the methylene position of the 2-ethyl group of the 2-ethyl-3-methylquinoline. The position to which the deuterium was transferred was not expected. None of the three pathways proposed in Scheme 1 can explain how deuterium would be shifted to this position. Also, the other ortho position and the para position of the aromatic ring were partially deuterated, which implies that both ortho and para positions are activated by a cobalt catalytic species. Only ortho C−H activation is involved in the conventional "Schiff base dimer" mechanism proposed by Watanabe (Species 6 in Scheme 1).[27]

As mentioned above, the reaction of the partially deuterated diallylaniline was much slower than the nondeuterated counterpart. This implies that a primary isotope effect involving cleavage of the ortho C−H or C−D bond must be present before or during the rate-limiting step. The primary isotopic effect can be determined by the reaction of a mixture of partially deuterated diallylaniline-d_5 and nondeuterated diallylaniline-d_0. Considering that a large isotope effect was expected, a reaction was run with a 5.61:1 mixture of partially deuterated diallylaniline-d_5 and nondeuterated diallylaniline-d_0. The reaction was monitored by GCMS over time. A large KIE of 5.4(1) was obtained, consistent

(37) Duff, E. J.; Queen, E. C. *J. Chem. Soc. A* **1968**, *8*, 1812.
(38) Dolgova, N. A.; Litvyak, I. G. *Izvestiya Akademii Nauk Kazakhskoi SSR, Seriya Khimicheskaya* **1986**, *5*, 23.

with the observations mentioned above regarding the rate of the reaction with diallylaniline-d_5 (Supporting Information).

Fully deuterated diallylaniline was prepared following the same procedure, providing reasonably pure fully deuterated diallylaniline-d_{15} (8% d_{14}-, 11% d_{13}- partially deuterated diallylanilines and 8% monoallylaniline-d_{10} were also present). Its reaction with $Co_2(CO)_8$ was examined. After 3 days, the final products were identified by combinations of ^{1}H NMR, ^{2}H NMR, and ^{13}C NMR spectroscopy as shown in eq 4 (Supporting Information). This result further confirmed the existence of a hydrogen shift from the arene to the methylene position, but again the mechanism in Scheme 1 cannot explain how this occurs.

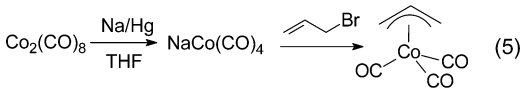


(4)

Mechanism of Quinoline Synthesis-C−N Cleavage. Since both monoallylaniline and aniline were observed in the reactions of diallylaniline, C−N bond cleavage must be occurring. A crossover reaction was conducted to determine whether the allyl exchange is reversible. Reaction of a 2:1 mixture of diallylaniline-d_{15} and diallylaniline-d_0 in the presence of $Co_2(CO)_8$ was carried out to partial completion. More diallylaniline-d_{15} was used because of the isotope effect on the reaction rate. The reaction was examined by GCMS after 5 h and seven peaks were detected and identified as monoallylaniline-d_{10}, monoallylaniline-d_0, deuteroaniline, aniline, and quinoline-d_0 as well as two starting materials. Failure to observe diallylaniline-d_5 and diallylaniline-d_{10} indicated that allyl exchange is not reversible in the starting material. It was also interesting that the deuterated isomers of a given compound can be separated by capillary GC (Supporting Information).

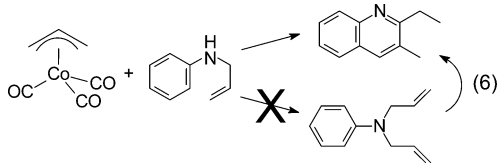
Isotope distribution was also examined after 19 h and at the end of the reaction (43 h total). ^{1}H NMR, ^{2}H NMR, and ^{13}C NMR spectroscopy of the final products indicated that there was mostly (94%) 2-ethyl-3-methylquinoline-d_0, and only a small quantity (6%) of 2-ethyl-3-methylquinoline-d_{13} was observed by ^{13}C NMR spectroscopy. Intermolecular allyl exchange would be expected as allylcobalttricarbonyl was observed during the reaction. In this case, d_4- and d_9-2-ethyl-3-methylquinoline would be formed as the intermolecular allyl transfer occurs between the substrates. However, because of the scrambling on the *o*- and *p*-phenyl group hydrogens at elevated temperatures, the final quinoline products ranged from d_0- to d_{13}-2-ethyl-3-methylquinoline, rendering a detailed analysis of the crossover products obscure. This experiment did demonstrate, however, that (a) crossover does occur and (b) the starting diallylaniline does not reversibly exchange allyl groups. Additional evidence for crossover comes from reaction of *N*-allyl-*N*-cinnamylaniline, which produces 2-ethyl-3-methylquinoline and 2-phenethyl-3-benzylquinoline in addition to the noncrossover product 3-methyl-2-phenethylquinoline.[2]

Mechanism of Quinoline Synthesis: Role of Allylcobalttricarbonyl. Since one key intermediate during the reaction was allylcobalttricarbonyl, this compound was synthesized directly and reacted with anilines to investigate its role in the formation of quinoline. The simple route shown in eq 5 was used to prepare allylcobalttricarbonyl, although there are additional routes reported in the literature.[39,40]



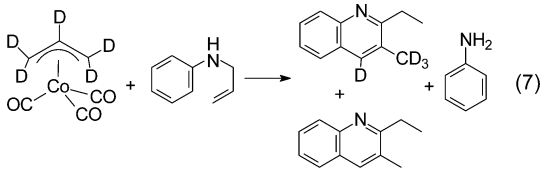
(5)

Allylcobalttricarbonyl is extremely volatile, so following its preparation all volatiles were transferred under vacuum to an ampule in a 1:1 ratio with monoallylaniline and heated to 105 °C (eq 6). No diallylaniline was detected during the reaction, and 2-ethyl-3-methylquinoline was directly formed, providing further confirmation that there is no allyl exchange between allylcobalttricarbonyl and monoallylaniline.



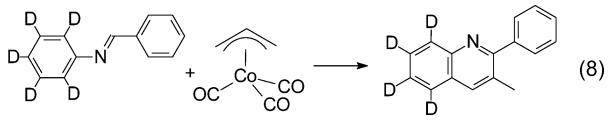
(6)

Allylcobalt tricarbonyl-d_5 was also prepared similarly and the reaction with monoallylaniline examined. Both d_0- and d_4-quinoline were observed in ~1:1 ratio from ^{1}H NMR spectroscopy (eq 7). Since no allyl exchange occurs between monoallylaniline and allylcobalttricarbonyl, it is possible that allylcobalttricarbonyl-d_5 reacts with monoallylaniline to form quinoline-d_4, and the ejected $Co(CO)_3$ reacted with monoallylaniline forming aniline and allylcobalttricarbonyl-d_0 species, which further reacted with monoallylaniline to form quinoline-d_0. Aniline is observed in the product mixture by GCMS.



(7)

In the above reactions, amines were used to react with allylcobalttricarbonyl. In order to investigate the reactivity of imines with allylcobalttricarbonyl, (E)-*N*-benzylideneaniline-d_5 was synthesized and was reacted with allylcobalttricarbonyl-d_0 (eq 8). Quinoline-d_4 was observed, which indicates that imines could serve as substrates/intermediates as suggested earlier.[1,2]



(8)

In eq 3, both ortho C−D and para C−D bonds were activated by a cobalt catalytic species. In order to test whether this species is allylcobalttricarbonyl, 1-phenylpyrrole was reacted with allylcobalttricarbonyl under similar conditions. 1-Phenylpyrrole was used to rule out the possibility that the nitrogen of the substrate assists allylcobalttricarbonyl in both ortho and para C−H activations. The resulting GCMS showed that two allyl addition/coupling products were produced at the ortho and para position of the phenyl ring, respectively. This result confirms

(39) Alper, H.; Abbayes, D. H.; Roches, D. D. *J. Organometal. Chem.* **1976**, *121*, 31.
(40) Heck, R. F. *J. Am. Chem. Soc.* **1963**, *85*, 4580.

Scheme 2. Proposed Mechanistic Sequence

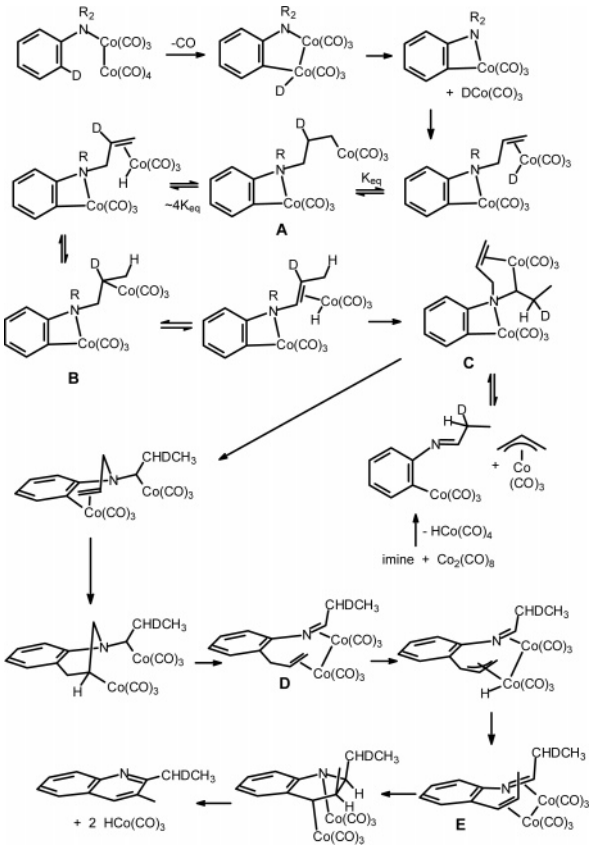
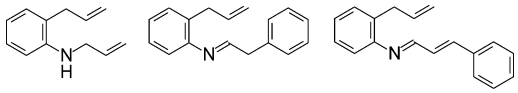


Chart 1. Three Possible Organic Intermediates



that allylcobalttricarbonyl undergoes both ortho and para C−H activations. This experiment further proved that allylcobalttricarbonyl can act as an allyl transfer reagent, and allylcobaltcarbonyl is one of the active intermediates that are involved in the ortho C−H activation leading to ring closure.

Some simple organic compounds shown in Chart 1 were also prepared,[41] which could be stable intermediates as suggested in Scheme 1. All three were reacted under the same reaction conditions as before with $Co_2(CO)_8$, but only traces of quinoline products were observed, arguing against these types of free species as active intermediates.

Proposed Mechanism. A proposed mechanism is shown in Scheme 2 based upon the isotopic labeling experiments described above. For simplicity, deuterium is shown only in one *o*-aryl position so that its migration path can be followed. The mechanism takes advantage of the isotopic preference for deuterium on carbon to account for the location of deuterium in the quinoline product. The reaction begins with the cleavage of the *o*-aryl C−D bond, which might be assisted by coordination of a $Co_2(CO)_7$ fragment to the nitrogen. Under the reaction conditions, CO will be labile in both $Co_2(CO)_8$ and $XCo(CO)_4$ species, so that vacant coordination sites form easily and reversibly. Indeed, a CO atmosphere is required at all times to keep the cobalt from depositing as cobalt metal. The hydride is eliminated as $DCo(CO)_3$ which then coordinates to and inserts into an allyl C−C double bond. The preference for a primary Co−C bond over a secondary Co−C bond leads to deuterium incorporation selectively at the β position of the alkyl group to form the intermediate **A**. This insertion is reversible, but the isotopic preference for deuterium on carbon (due to a lower zero point energy contribution to the energy) leads to β-elimination of a C−H bond. The reversibility of this reaction leads to a thermodynamic equilibrium with $K_{eq} \approx 4-5$, which accounts for the observed 85% HD in this position in the quinoline product. Occasionally, the insertion proceeds to give a secondary Co−C isomer **B** which can β-eliminate in the other direction to give an enamine. Reinsertion places the cobalt α to the nitrogen in **C**, and from here β-carbon elimination of the allyl group occurs, perhaps through an S_N2' mechanism, to produce imine plus π-allylcobalttricarbonyl. Note that use of imine as starting material can also lead convergently to this same intermediate, **C**. From the intermediate **C**, the allyl group can bridge to a second cobalt in the *o*-aryl position where olefin insertion is followed by another β-carbon elimination to regenerate the imine and a cobalt-olefin complex **D**. The double bond can isomerize via a π-allylhydride intermediate to a *cis*-olefin−imine complex **E**, at which point reductive coupling leads to the formation of the second six-membered ring. Importantly, this coupling also produces a product in which the two cobalts are cis to adjacent hydrogens, permitting β-elimination to give the quinoline product and $HCo(CO)_3$. The latter can combine to produce H_2, undergo C−H exchange with the arene in the ortho and para positions, or react with diallylaniline to give monoallylaniline and π-allylcobalttricarbonyl. This mechanism, while still speculative, accounts for all intermediates and labeling results using known reactions of cobalt carbonyls.

Conclusions

In conclusion, 2,3-substituted quinolines are readily synthesized with the use of a commercially available catalyst and convenient starting materials under mild reaction conditions. The yields range from fair to good, depending on the substituents present. Electron-donating functional groups on the aromatic rings of the diallylanilines favor the reaction both by weakening the C−N bond by stabilizing the imine intermediate that is formed and also by making the C−H activation step faster. Conversely, electron-withdrawing functional groups on the aromatic rings of the diallylanilines slow the reaction. Steric effects predominate over electronic effects. Ortho substitutions slow down the entire reaction by blocking ring closure to form the quinoline skeletons. Isotopic labeling experiments provide some insights into the details of the mechanism, allowing a complete mechanism to be proposed that accounts for the experimental observations and provides a rational route to the products using established steps.

Experimental Section

General Information. Cobalt carbonyl was purchased from Strem and used as received. CO was purchased from Air Products. Allyl bromide-d_5 was purchased from CDN Isotopes, and deuteroaniline was purchased from Aldrich. *N*-allylmethylamine was purchased from Aldrich and used as received. THF was distilled over sodium/benzophenone and degassed prior to use. All other compounds except the diallylanilines were synthesized as previously reported.[39−41]

(41) Boholz, L. G.; Stille, J. R. *J. Org. Chem.* **1983**, *58*, 5095.

All NMR spectra were recorded on a Bruker AMX400 spectrometer, an AVANCE400 spectrometer, or an AVANCE500 spectrometer. GC-MS was conducted on a Shimadzu QP-2010 spectrometer.

Procedure for the Reaction of *N*-Allylmethylamine. In a 50-mL ampule equipped with a Teflon seal, 71.1 mg of *N*-methylallylamine (1.00 mmol) and 24.3 mg of $Co_2(CO)_8$ (0.0711 mmol) were added to 5 mL of dry THF in a glove box. Any dissolved nitrogen was removed by freeze−pump−thaw degassing three times on a Schlenk line. Carbon monoxide was then introduced at 1 atm, and the reaction mixture was heated at 120 °C in an oil bath for 5 days with stirring. The catalyst was removed by passing the reaction solution through an alumina column followed by column chromatography to isolate the product (silica gel, J.T. Baker, 40−140 mesh, 25% ethyl acetate/hexane as eluent). The isolated yield of light yellow oily 1-methylpyrrolidin-2-one was 72.0 mg (0.73 mmol, 73%). ^{1}H NMR: δ 3.35 (t, 2H, J = 7.2 Hz), 2.81 (s, 3H), 2.34 (t, 2H, J = 8.0 Hz), 1.99 (tt, 2H, J = 8.0, 7.2 Hz). ^{13}C NMR: δ 175.03, 49.40, 30.66, 29.55, 17.64.

General Procedure for the Synthesis of Diallylaniline from Aniline. In a 50-mL round-bottom flask fitted with a reflux condenser and stir bar, 0.91 mL of aniline (9.8 mmol), 1.99 mL of allyl bromide (0.023 mol), and 1.06 g Na_2CO_3 (0.01 mol) were added to 32 mL of ethanol and 8 mL of H_2O and refluxed overnight. The crude product was extracted with diethyl ether and concentrated, dried over anhydrous $MgSO_4$, and distilled over potassium hydroxide to provide colorless diallylaniline (1.60 g, 9.3 mmol, 93%).

General Procedure for the Conversion of Diallylanilines to Quinolines. In a 50-mL ampule equipped with a Teflon seal, 173 mg of diallylaniline (1.00 mmol) and 24.3 mg of $Co_2(CO)_8$ (0.0711 mmol) were added to 5 mL of dry THF in a glove box. Any dissolved nitrogen was removed by freeze−pump−thaw degassing three times on a Schlenk line. Carbon monoxide was then introduced at 1 atm, and the reaction mixture was heated at 105 °C in an oil bath for 48 h with stirring (Caution: the pressure exceeds 1 atm and should be kept behind a shield!). The catalyst was removed by passing the reaction solution through an alumina column, and the product isolated by column chromatography (silica gel, J.T. Baker, 40−140 mesh, 10% ethyl acetate/hexane as eluent). The isolated yield of light yellow oily 2-ethyl-3-methylquinoline was 111.3 mg (0.65 mmol, 65%). The following quinolines were prepared using this methodology. Isolated yields of quinolines are listed in Table 1.

2-Ethyl-3-methylquinoline (entry 1, Table 1). ^{1}H NMR: δ 8.02 (d, 1H, J = 8.4 Hz), 7.84 (s, 1H), 7.70 (d, 1H, J = 8.0 Hz), 7.61 (dd, 1H, J = 8.0, 7.2 Hz), 7.44 (dd, 1H, J = 7.6, 7.2 Hz), 3.01 (q, 2H, J = 7.6 Hz), 2.49 (s, 3H), 1.37 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 163.29, 146.67, 135.73, 129.40, 128.52, 128.28, 127.33, 126.69, 125.59, 29.49, 19.09, 12.85. Oily liquid.

2-Ethyl-3,6,8-trimethylqunniloline (entry 2, Table 1). ^{1}H NMR: δ 7.68 (s, 1H), 7.28 (s, 1H), 7.26 (s, 1H), 2.97 (q, 2H, J = 7.6 Hz), 2.77 (s, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 1.41 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 160.46, 144.14, 137.79, 136.19, 134.82, 130.45, 128.95, 127.12, 123.42, 29.06, 21.45, 18.94, 17.61, 12.10. White solid.

2-Ethyl-3,7,8-trimethylquinoline (entry 3, Table 1). ^{1}H NMR: δ 7.73 (s, 1H), 7.45 (d, 1H, J = 7.6 Hz), 7.25 (d, 1H, J = 7.2 Hz), 2.97 (q, 2H, J = 7.6 Hz), 2.77 (s, 3H), 2.48 (s, 3H), 2.44 (s, 3H), 1.44 (t, 3H, J = 7.2 Hz). ^{13}C NMR: δ 161.16, 145.48, 135.54, 135.32, 133.86, 128.22, 127.88, 125.37, 123.49, 29.17, 20.49, 18.79, 13.04, 12.02. White solid.

2-Ethyl-3,5,7-trimethylquinoline (entry 4, Table 1). ^{1}H NMR: δ 7.93 (s, 1H), 7.68 (s, 1H), 7.12 (s, 1H), 2.98 (q, 2H, J = 7.6 Hz), 2.61 (s, 3H), 2.49 (s, 3H), 2.48 (s, 3H), 1.37 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 162.54, 147.16, 137.80, 133.05, 132.12, 128.33, 127.86, 125.88, 124.51, 29.36, 21.66, 19.27, 18.43, 12.84. White solid.

2-Ethyl-5,7-dimethoxy-3-methylquinoline (entry 5, Table 1). ^{1}H NMR: δ 8.11 (s, 1H), 6.96 (d, 1H, J = 1.8 Hz), 6.44 (d, 1H, J = 1.9 Hz), 3.94 (s, 3H), 3.92 (S, 3H), 2.94 (q, 2H, J = 7.6 Hz), 2.44 (s, 3H), 1.34 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 163.84, 160.30, 155.49, 148.64, 130.65, 126.05, 115.36, 99.20, 97.27, 55.67, 55.54, 29.54, 18.97, 13.00. MS: *m*/*e* 231, 230(bp), 215, 188, 172, 158, 145, 130, 115, 102, 89, 77. White solid.

2-Ethyl-3,5,8-trimethylquinoline (entry 6, Table 1). ^{1}H NMR: δ 8.00 (s, 1H), 7.39 (d, 1H, J = 6.8 Hz), 7.21 (d, 1H, J = 6.8 Hz), 3.04 (q, 2H, J = 7.2 Hz), 2.82 (s, 3H), 2.66 (s, 3H), 2.55 (s, 3H), 1.43 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 160.71, 145.72, 134.57, 131.99, 130.99, 128.43, 127.73, 126.27, 125.61, 29.08, 19.22, 18.42, 17.77, 12.08. White solid.

2-Ethyl-3,8-dimethylquinoline (entry 7, Table 1). ^{1}H NMR: δ 7.78 (s, 1H), 7.53 (d, 1H, J = 8.4 Hz), 7.44 (d, 1H, J = 7.2 Hz), 7.32 (dd, 1H, J = 7.6, 7.2 Hz), 2.98 (q, 2H, J = 7.4 Hz), 2.80 (s, 3H), 2.46 (s, 3H), 1.42 (t, 3H, J = 7.4 Hz). ^{13}C NMR: δ 161.41, 145.54, 136.63, 135.39, 129.03, 128.16, 127.04, 125.16, 124.55, 29.17, 18.93, 17.75, 12.05. Oily liquid.

2-Ethyl-3,6-dimethylquinoline (entry 8, Table 1). ^{1}H NMR: δ 7.91 (d, 1H, J = 8.4 Hz), 7.74 (s, 1H), 7.45 (d, 1H, J = 1.6 Hz), 7.42 (dd, 1H, J = 8.8, 1.6 Hz), 2.97 (q, 2H, J = 7.6 Hz), 2.50 (s, 3H), 2.47 (s, 3H), 1.36 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 162.20, 145.21, 135.13, 135.07, 130.42, 129.22, 128.18, 127.28, 125.53, 29.36, 21.44, 19.04, 12.82. Oily liquid.

2-Ethyl-3-methyl-6-methoxyquinoline (entry 9, Table 1). ^{1}H NMR: δ 7.97 (d, 1H, J = 8.8 Hz), 7.73 (s, 1H), 7.27 (dd, 1H, J = 8.8, 2.8 Hz), 6.97 (d, 1H, J = 2.8 Hz), 3.90 (s, 3H), 2.95 (q, 2H, J = 7.6 Hz), 2.46 (s, 3H), 1.35 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 160.62, 157.09, 142.63, 134.72, 129.90, 129.58, 128.08, 120.58, 104.46, 55.36, 29.17, 19.03, 12.85. White solid.

2-Ethyl-3,8-dimethyl-6-methoxyquinoline (entry 10, Table 1). ^{1}H NMR: δ 7.67 (s, 1H), 7.12 (d, 1H, J = 1.6 Hz), 6.82 (d, 1H, J = 2.8 Hz), 3.88 (s, 3H), 2.94 (q, 2H, J = 7.6 Hz), 2.43 (s, 3H), 1.40 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 158.83, 156.63, 141.82, 138.43, 134.52, 129.36, 127.94, 120.36, 102.28, 55.20, 28.88, 18.92, 17.71, 12.13. MS: *m*/*e* 215, 214(bp), 200, 187, 171, 157, 144, 128, 115, 91, 77. White solid.

2-Ethyl-3-methyl-6-trifluoromethylquinoline (entry 11, Table 1). ^{1}H NMR: δ 8.10 (d, 1H, J = 8.8 Hz), 8.01 (s, 1H), 7.90 (s, 1H), 7.78 (dd, 1H, J = 8.8, 2.0 Hz), 3.01 (q, 2H, J = 7.2 Hz), 2.51 (s, 3H), 1.38 (t, 3H, J = 7.6 Hz). ^{13}C NMR: δ 165.69, 147.56, 136.14, 130.95, 129.62, 127.24, 126.18, 125.53, 124.60, 123.91, 29.51, 19.08, 12.44. MS: *m*/*e* 239, 238(bp), 211, 190, 167, 140, 115, 87, 63. Light yellow solid.

Preparation of Diallylaniline-d_5 from Deuteroaniline. In a 25-mL ampule fitted with a reflux condenser and stir bar, 100 μL of deuteroaniline (1.1 mmol), 238 μL of allyl bromide (2.5 mmol), and 116 mg of Na_2CO_3 (1.1 mmol) were added to 8 mL of EtOD and 2 mL of D_2O and refluxed overnight. The crude product was extracted with diethyl ether and concentrated, dried over anhydrous $MgSO_4$, and distilled to provide colorless diallylaniline-d_5 (172 mg, 0.967 mmol, 87.9%).

Preparation of Diallylaniline-d_{15} from Deuteroaniline. The procedure was the same as for preparation of diallylaniline-d_5 except that 238 μL of allyl bromide-d_5 was used and refluxed for 60 h to provide colorless diallylaniline-d_{15} (166 mg, 0.883 mmol, 80.3%). GCMS analysis showed the product to contain 8% d_{14}-diallylaniline, 11% d_{13}-diallylaniline, and 8% monoallylaniline-d_{10}.

Procedure for the Conversion of Diallylaniline-d_5, Diallylaniline-d_{15} to Quinolines. In a 25-mL ampule equipped with a Teflon seal, 17.8 mg of diallylaniline-d_5 (0.1 mmol) or 18.8 mg of diallylaniline-d_{15} (0.1 mmol) and 8.5 mg of $Co_2(CO)_8$ (0.025 mmol) were added to 5 mL of dry THF in a glove box. Any dissolved nitrogen was removed by freeze−pump−thaw degassing three times on a Schlenk line. Carbon monoxide was then introduced at 1 atm, and the reaction mixture was heated at 105 °C in an oil bath for 55 h with stirring. The catalyst was removed by passing the reaction solution through an alumina column, and THF was removed under vacuum followed by NMR analyses

directly without any purification. The spectra are described in the text and shown in the Supporting Information.

Procedure for the Reaction of Diallylaniline-d_5 and Diallylaniline-d_0. In a 25-mL ampule equipped with a Teflon seal, 2.8 mg of diallylaniline-d_0 (0.016 mmol), 16.2 mg of diallylaniline-d_5 (0.091 mmol), and 3.7 mg of $Co_2(CO)_8$ (0.011 mmol) were added to 5 mL of dry THF in a glove box. Any dissolved nitrogen was removed by freeze−pump−thaw degassing three times on a Schlenk line. Carbon monoxide was then introduced at 1 atm, and the reaction mixture was heated at 105 °C in an oil bath for 6 h with stirring. The reaction flask was taken into the glove box and an aliquot was removed for GCMS analysis after passing through an alumina column. The reaction flask was then taken out of the glove box and freeze−pump−thaw degassed three times, and 1 atm of CO was introduced on the Schlenk line. The flask was heated in an oil bath for additional 6 h. The same procedure was repeated after 14 and 16 h. The calculation of the primary isotopic effect is described in the Supporting Information.

Crossover Experiment. In a 25-mL ampule equipped with a Teflon seal, 37.6 mg of diallylaniline-d_{15} (0.2 mmol), 17.8 mg diallylaniline-d_5 (0.1 mmol), and 25.5 mg of $Co_2(CO)_8$ (0.0737 mmol) were added to 15 mL of dry THF in a glove box. Any dissolved nitrogen was removed by freeze−pump−thaw degassing three times on a Schlenk line. Carbon monoxide was then introduced at 1 atm, and the reaction mixture was heated at 105 °C in an oil bath for 5 h with stirring. The reaction flask was taken into the glove box, and an aliquot was removed for GCMS analysis after passing through an alumina column. The reaction flask was then taken out of the glove box and freeze−pump−thaw degassed three times, and 1 atm of CO was introduced on the Schlenk line. The flask was heated in an oil bath for additional 14 h. An aliquot was again removed for analysis and the flask heated for additional 24 h. The catalyst was removed by passing the reaction solution through an alumina column, and THF was removed under vacuum followed by GCMS and NMR analyses directly without any further purification. The spectra are described in the text and shown in the Supporting Information.

General Procedure for the Reaction of Allylcobalttricarbonyl. In a 50-mL two neck ampule, 19.4 mg of $NaCo(CO)_4$ (0.1 mmol) was added to 5 mL of dry THF in a glove box. In a dry ice/acetone bath with stirring, allyl bromide (9 μL, 0.1 mmol) was added slowly and then warmed to room temperature. The yellow volatile allylcobalttricarbonyl was vacuum transferred to another 50-mL ampule equipped with a Teflon seal and 13.3 mg monoallylaniline (0.1 mmol). Any dissolved nitrogen was removed by freeze−pump−thaw degassing three times on a Schlenk line. Carbon monoxide was then introduced at 1 atm, and the reaction mixture was heated at 105 °C. The metal salt was removed by passing the reaction solution through an alumina column, and THF was removed under vacuum followed by GCMS and NMR analyses directly without any further purification.

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Supporting Information Available: Includes NMR spectra and detailed GC-MS determinations for the quinoline-forming reaction and the deuterated reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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